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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte MARK E. COOK and DAN E. BUTZ

Appeal 2009-005347[1]
Application 10/756,719
Technology Center 1600

Decided: December 22, 2009

Before TONI R. SCHEINER, DEMETRA J. MILLS, and FRANCISCO C. PRATS, *Administrative Patent Judges*.

PRATS, *Administrative Patent Judge*.

DECISION ON APPEAL

This appeal under 35 U.S.C. § 134 involves claims to a method of treating rheumatoid arthritis with conjugated linoleic acid. The Examiner rejected the claims as obvious.

We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

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[1] The Wisconsin Alumni Research Foundation is the real party in interest.

STATEMENT OF THE CASE

"Conjugated linoleic acid ('CLA') is a group of positional and geometrical isomers of linoleic acid. . . . These naturally occurring fatty acids are found in beef and dairy products due to ruminal isomerization of linoleic acid" (Spec. [0003] (citations omitted)). According to the Specification, "CLA has been shown to modulate immune response" in prior art studies (*id.* at [0006] (citations omitted)).

The Specification discloses that, in a mouse model for human rheumatoid arthritis, "mice fed CLA had significantly lower arthritis severity scores as compared to mice fed corn oil" (*id.* at [00025]), the scores being based on redness and swelling of the ankle or wrist (*id.* at [00023]).

Claims 3 and 5-16 stand rejected and appealed (App. Br. 2). Claim 3, the only independent claim, and claim 5 are representative and read as follows:

> 3. A method for treating rheumatoid arthritis in a human or non-human animal in need thereof, the method comprising the steps of:
>
> administering to the human or non-human animal a composition that consists of a conjugated linoleic acid (CLA) and one or more carriers wherein the CLA is in an amount effective to reduce joint inflammation in the human or non-human animal; and
>
> observing an improvement in joint redness and swelling in the human or non-human animal.
>
> 5. The method of claim 3, wherein the CLA is selected from a free conjugated linoleic acid, an ester of a conjugated linoleic acid, a non-toxic salt of a conjugated linoleic acid, an active isomer of a conjugated linoleic acid, an active metabolite of a conjugated linoleic acid, and a mixture thereof.

The Examiner cites the following documents as evidence of unpatentability:

Horrobin	US 6,245,811 B1	Jun. 12, 2001
Cook	US 6,395,782 B1	May 28, 2002

The sole rejection before us for review is the Examiner's rejection of claims 3 and 5-16 as being unpatentable under 35 U.S.C. § 103(a) over Cook and Horrobin (Ans. 3-6).

OBVIOUSNESS

ISSUE

The Examiner cites Cook as disclosing administration of conjugated linoleic acid to treat autoimmune disorders, including rheumatoid arthritis (Ans. 3-4). The Examiner cites Horrobin as disclosing administration of esters of conjugated linoleic acid, also for treating rheumatoid arthritis (*id.* at 4).

Based on these teachings the Examiner concludes that an ordinary artisan would have considered it obvious "to use an ester of conjugated linoleic acid, as suggested by Horrobin et al., in the method of treating rheumatoid arthritis as taught by Cook et al. and produce the instant invention" (*id.* at 5).

Appellants contend that the Examiner erred in interpreting the teachings in the prior art because neither Cook nor Horrobin "teach the element of 'improvement in joint redness and swelling' recited in independent claim 3" (App. Br. 4; *see also* App. Br. 6, 10). Thus, Appellants argue, if the Examiner meant that "conjugated linoleic acid would inherently reduce joint redness and swelling, this is a legal mistake in that what is inherent in the prior art, if not known at the time of the

invention, cannot form a proper basis for rejecting the claimed invention as obvious under § 103" (*id.* at 5 (citing *In re Shetty*, 566 F.2d 81, 86 (CCPA 1977)); *see also* App. Br. 8).

Appellants argue that "the evidence on the record supports that an ester of conjugated linoleic acid is unlikely to reduce joint redness and swelling even assuming it can extend the survival time and reduce body weight wasting" as taught by Cook (App. Br. 6). Specifically, Appellants urge,

> it is not uncommon that a treatment of a condition reduces some but not all symptoms of the condition. For example, a patient suffering from a common cold may experience fever, pain, nasal congestion, excess cough and other symptoms. Acetaminophen can reduce fever and pain but not other symptoms. Similarly, decongestants will reli[e]ve congestion but not other symptoms.

(*Id.* at 7.) Therefore, Appellants argue, "just because Cook et al. taught that conjugated linoleic acid can extend the survival time and reduce body weight wasting does not mean that it can also reduce joint redness and swelling" (*id.*).

Appellants further argue, as evidenced by Yang's[2] disclosure of conjugated linoleic acid promoting the early onset of proteinuria in the same mouse model used by Cook, that the claimed therapeutic agent was known to promote rather than reduce certain symptoms of lupus erythematosus (*id.* at 8-9). Moreover, Appellants argue, given that rheumatoid arthritis

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[2] Mingder Yang et al., *Dietary Conjugated Linoleic Acid Protects Against End Stage Disease of Systemic Lupus Erythematosus in the NZB/W F1 Mouse*, 22 IMMUNOPHARMACOLOGY AND IMMUNOTOXICOLOGY 433-449 (2000).

involves deposition of antibody/antigen immune complexes, an ordinary artisan viewing the disclosures by Sugano[3] and Yamasaki[4] that conjugated linoleic acid increases antibody production "would not conclude with a reasonable likelihood of success based on the teachings of Cook et al. that conjugated linoleic acid can reduce joint redness and swelling in rheumatoid arthritis" (*id.* at 10 (citing Cook et al., U.S. Patent No. 5,428,072, issued Jun. 27, 1995) (hereinafter "Cook '072")).

Appellants further contend that the Examiner erred in interpreting Horrobin as teaching or suggesting administering conjugated linoleic acid for treating rheumatoid arthritis, because Horrobin teaches numerous fatty acids as being useful treating a number of different disorders (App. Br. 11-12). Appellants therefore conclude that, when all of the relevant prior art is considered, "it would not have been obvious to one of ordinary skill in the art that conjugated linoleic acid can be used to reduce joint redness and swelling in rheumatoid arthritis" (*id.* at 15).

In view of the positions advanced by Appellants and the Examiner, the issue with respect to this rejection is whether Appellants have shown that the Examiner erred in concluding that an ordinary artisan viewing the teachings of Cook and Horrobin, as well as the other relevant prior art teachings, would have considered it obvious to treat rheumatoid arthritis

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[3] Michihiro Sugano et al., *Conjugated Linoleic Acid Modulates Tissue Levels of Chemical Mediators and Immunoglobulins in Rats*, 33 LIPIDS 521-27 (1998).

[4] Masao Yamasaki et al., *Immunoglobulin and Cytokine Production from Spleen Lymphocytes Is Modulated in C57BL/6J Mice by Dietary Cis-9, Trans-11 and Trans-10, Cis-12 Conjugated Linoleic Acid*, 133 J. NUTR. 784-88 (2003).

with conjugated linoleic acid, or esters of conjugated linoleic acid, as recited in the claims.

FINDINGS OF FACT ("FF")

1. Cook discloses a "method for extending the survival time of a human or non-human animal having an autoimmune complex disease [which] includes the step of administering to the animal after diagnosis of the autoimmune complex disease an amount of CLA [(conjugated linoleic acid)] effective to extend the life span of the animal" (Cook, col. 2, ll. 34-39).

2. Cook discloses that its methods "are not limited to use in human SLE [(systemic lupus erythematosus)] patients (or equivalent diseases in non-human animals)" (*id.* at col. 3, ll. 37-39). Rather,

> [t]he methods are of *particular use* in other autoimmune diseases and conditions including but not limited to *arthritis*, multiple sclerosis, Addison's disease, Goodpastures's syndrome, Graves' disease, Hashimoto's thyroiditis, insulin-dependent diabetes mellitus, myasthenia gravis, myocardial infarction, poststreptococcal glomerulonephritis, spontaneous infertility, ankylosing spondylitis, *rheumatoid arthritis*, scleroderma, and Sjogren's syndrome.

(*Id.* at col. 3, ll. 43-50 (emphases added).)

3. Cook acknowledges the disclosure in Yang that "dietary CLA fed from weaning onward accelerates the onset of proteinuria but does not significantly affect anti-DNA antibody production in those same mice. In the same study, the CLA-fed mice lived longer from the onset of proteinuria and lost less body weight than control mice" (Cook, col. 2, ll. 17-20).

4. Horrobin discloses preparing therapeutically active molecules by covalently binding together two individual compounds known to have desirable biological activities, using ester linkages (Horrobin, col. 1, ll. 18-

20). "For example, a bioactive alcohol may be coupled to an unsaturated fatty acid as an ester/ether via a geminal dioxo linkage" (*id.* at col. 2, ll. 23-25).

5. Horrobin discloses that fatty acids useful in its methods include GLA (gamma linoleic acid), DGLA (dihomo gamma linoleic acid), and conjugated linoleic acid (*id.* at col. 5, l. 54, through col. 6, l. 39).

6. According to Horrobin:

> In their own right GLA and DGLA have been shown to have anti-inflammatory effects, to lower blood pressure, to inhibit platelet aggregation, to lower cholesterol levels, to inhibit cancer cell growth, to reduce dyskinetic movements, to relieve brea[s]t pain, to improve calcium absorption and enhance its deposition in bone, to reduce the adverse effects of ionising radiation, to treat various psychiatric disorders, to cause vasodilation, to improve renal function, to treat the complications of diabetes, to dilate blood vessels and so on. *Actives linked to GLA and DGLA will therefore not only become more lipophilic, enhancing penetration across all membranes, the skin and the blood brain barrier, but are also likely to exhibit new additional therapeutic effects.*

(*Id.* at col. 6, ll. 15-27 (emphasis added).)

7. Horrobin discloses that the anti-inflammatory effects of GLA and DLA render them suitable for the treatment of various disorders, including "osteoarthritis and rheumatoid arthritis" (*id.* at col. 13, ll. 30-31; *see also* col. 13, ll. 60-64)

8. Horrobin discloses that conjugated linoleic acid is also a fatty acid "of particular interest" in the disclosed methods, given its "effects in treating and preventing cancer, in promoting growth particularly of protein-containing tissues, in preventing and treating cardiovascular disease and as an antioxidant" (*id.* at col. 6, ll. 34-39).

9. One passage at issue in Horrobin reads as follows:

> It is thus apparent that various specific fatty acids are likely to be able to add to the efficacy of drugs and other bioactive substances of almost any class, in both the treatment and prevention of disease, in skin care and in nutrition, as well as having valuable therapeutic effects when given in the form as now proposed by the present invention as a single fatty acid or as two different fatty acids in the same molecule. Of particular value in therapy is that under most circumstances the fatty acids are remarkably non-toxic and can be administered safely in large doses without the risk of important side effects.
>
> Specific Uses of Compounds Containing Geminal Dioxo or Geminal Amino Oxo Linkage(s)
>
> 1. Geminal dioxo or geminal amino oxo moiety-containing compounds containing: two fatty acids in which one fatty acid is GLA or DGLA and the other is GLA, DGLA, SA, EPA, DHA, cLA (conjugated linoleic acid) or CA (columbinic acid) for the treatment of:
>
> (a) complications of diabetes, particularly neuropathy and retinopathy; and improvement of responses to insulin in diabetes and pre-diabetes;
>
> (b) cancers;
>
> (c) osteoarthritis;
>
> *(d) rheumatoid arthritis;*
>
> (e) other inflammatory and auto-immune diseases including Sjogren's syndrome, systemic lupus, ulcerative colitis, Crohn's disease and uveitis; respiratory diseases including asthma;
>
> (g) neurological disorders including multiple sclerosis, Parkinson's disease and Huntington's chorea;
>
> (h) renal and urinary tract disorders;
>
> (i) cardiovascular disorders;
>
> (j) degenerative diseases of the eye including retinitis pigmentosa and
> senile macular degeneration;

> (k) psychiatric disorders including schizophrenia, Alzheimer's disease, attention deficit disorder, alcoholism and depression;
> (l) prostatic hypertrophy and prostatitis;
> (m) impotence and male infertility;
> (n) mastalgia;
> (o) male pattern baldness;
> (p) osteoporosis;
> (q) dermatological disorders, including atopic eczema, hand eczema, psoriasis, urticaria and allergic disorders;
> (r) dyslexia and other learning disabilities;
> (s) cancer cachexia.

(*Id.* at col. 14, l. 44, through col. 15, l. 25 (emphasis added).)

10. Yang investigated "the influence of dietary CLA on immune disorders in the SLE-prone NZB/W F1 mice" (Yang 435).

11. Yang found that dietary CLA "accelerated the onset of proteinuria in autoimmune-prone NZB/W F1 mice but did not affect anti-DNA antibody production" (*id.* at 433 (abstract)). Yang ultimately concluded that its data "suggested that dietary CLA may accelerate the autoimmune symptoms of NZB/W F1 mice, however, CLA protected against the disease related body weight loss and prolonged survival after proteinuria" (*id.*).

12. Yamasaki "evaluated the effect of *cis*-9, *trans*-11 (9c, 11 t) and *trans*-10, *cis*-12 (10t, 12c) conjugated linoleic acid (CLA) on the immune system in C57BL/6J mice" (Yamasaki 784 (abstract)).

13. Yamasaki discloses that relative spleen weights "of all CLA fed mice were greater than the controls. Spleen lymphocytes isolated from the mice fed 10t, 12c-CLA produced more immunoglobulin (Ig)A and IgM but not IgG when stimulated with concanavalin A (ConA) compared with controls" (*id.*).

14. Yamasaki states that its results suggest that "9c, 11t and 10t, 12c-CLA can stimulate different immunological effects and that the simultaneous intake of the two isomers can change the T cell population" (*id.*).

15. Sugano examined the "effects of conjugated linoleic acid (CLA) on the levels of chemical mediators in peritoneal exudate cells, spleen and lung, and the concentration of immunoglobulins in mesenteric lymph node and splenic lymphocytes and in serum" in rats (Sugano 521).

16. Sugano discloses:

> Splenic levels of immunoglobulin A (IgA), IgG, and IgM increased while those of IgE decreased significantly in animals fed the 1.0% CLA diet. This was reflected in the serum levels of immunoglobulins. The levels of IgA, IgG, and IgM in mesenteric lymph node lymphocytes increased in a dose dependent manner, while IgE was reduced in those fed the higher CLA intake. However, no differences were seen in the proportion of T-lymphocyte subsets of mesenteric lymph node. These results support the view that CLA mitigates the food-induced allergic reaction.

(*Id.*)

17. Cook '072 discloses a "method of enhancing weight gain and feed efficiency in an animal which comprises administering to the animal a safe and effective amount of a conjugated linoleic acid" (Cook '072, abstract).

PRINCIPLES OF LAW

In *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398 (2007), the Supreme Court rejected a rigid approach to the question of obviousness, and ultimately reaffirmed that "when a patent 'simply arranges old elements with each performing the same function it had been known to perform' and yields no more than one would expect from such an arrangement, the combination

is obvious." *Id.* at 417 (quoting *Sakraida v. Ag Pro, Inc.*, 425 U.S. 273 (1976)).

The Court also cautioned that, "[i]n determining whether the subject matter of a patent claim is obvious, neither the particular motivation nor the avowed purpose of the patentee controls. What matters is the objective reach of the claim. If the claim extends to what is obvious, it is invalid under § 103." *Id.* at 419.

Ultimately, therefore, as our reviewing court has stated, "[i]n determining whether obviousness is established by combining the teachings of the prior art, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art." *In re GPAC Inc.*, 57 F.3d 1573, 1581 (Fed. Cir. 1995) (internal quotations omitted).

Nonetheless, a prima facie case of obvious cannot be based on a fact not disclosed in the prior art. *See In re Rijckaert*, 9 F.3d 1531, 1534 (Fed. Cir. 1993) ("'That which may be inherent is not necessarily known. Obviousness cannot be predicated on what is unknown.' Such a retrospective view of inherency is not a substitute for some teaching or suggestion supporting an obviousness rejection.") (quoting *In re Spormann*, 363 F.2d 444, 448 (CCPA 1966)).

On the other hand, the inherent properties of prior art elements need not be disclosed in the prior art. *See In re Woodruff*, 919 F.2d 1575, 1577-78 (Fed. Cir. 1990) (obviousness rejection affirmed where using claimed elements in the manner suggested by the prior art necessarily resulted in claim-recited effect); *see also MEHL/Biophile Int'l Corp. v. Milgraum,* 192 F.3d 1362, 1365 (Fed. Cir. 1999) ("Inherency is not necessarily coterminous with knowledge of those of ordinary skill in the art. Artisans of ordinary

skill may not recognize the inherent characteristics or functioning of the prior art."); *In re Baxter-Travenol Labs.*, 952 F.2d 388, 392 (Fed. Cir. 1991) ("Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention.").

ANALYSIS

Appellants' arguments do not persuade us that the Examiner erred in concluding that an ordinary artisan viewing the teachings of Cook and Horrobin, as well as the other relevant prior art teachings, would have considered it obvious to treat rheumatoid arthritis with conjugated linoleic acid, or esters of conjugated linoleic acid, as recited in the claims.

As the Examiner points out, Cook discloses that conjugated linoleic acid was known to be useful for treating rheumatoid arthritis (FF 2). The Examiner does not, however, appear to dispute Appellants' contention that Cook fails to explicitly disclose that its treatment improves the disorder's swelling and redness.

Thus, it might be true that Appellants' stated rationale for treating rheumatoid arthritis with CLA, reducing swelling and redness, is different than the prior art's reason. That fact, however, does not render the claimed process any less obvious, given Cook's direct and explicit disclosure that CLA is useful for treating rheumatoid arthritis. *See KSR*, 550 U.S. at 419 ("In determining whether the subject matter of a patent claim is obvious, neither the particular motivation nor the avowed purpose of the patentee controls.").

Moreover, we are not persuaded that Horrobin fails to suggest administering esters of CLA for treating rheumatoid arthritis. Horrobin discloses that compounds in which GLA or DGLA is esterified to another

fatty acid, which can be CLA, are useful in the treatment of, among other diseases, rheumatoid arthritis (*see* FF 9). While it might be true that CLA is not among the fatty acids disclosed by Horrobin as being useful for treating rheumatoid arthritis, both GLA and DGLA are disclosed as being useful in such a treatment method (*see* FF 7).

Thus, because GLA and DGLA are disclosed as being useful for treating rheumatoid arthritis, we agree with the Examiner that an ordinary artisan viewing Horrobin's disclosure would have reasoned that GLA and/or DGLA esterified with CLA would also be useful in treating rheumatoid arthritis, particularly given Horrobin's listing of that disorder among the treatable diseases, and further given Cook's disclosure of using CLA to treat rheumatoid arthritis.

Thus, the rationale for practicing the administering and observing steps recited in claim 3 is the express disclosure in both of the cited references that the claimed therapeutic agents are useful for treating the claimed disorder. We are therefore not persuaded that the Examiner has improperly used any undisclosed inherent properties of CLA or CLA esters in finding that an ordinary artisan would have been prompted to treat rheumatoid arthritis with those agents.

Moreover, with respect to the claimed effect of improvement in joint redness and swelling, "[m]ere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention." *In re Baxter-Travenol Labs.*, 952 F.2d 388, 392 (Fed. Cir. 1991); *cf. In re Woodruff*, 919 F.2d at 1577-78 (Fed. Cir. 1990) (obviousness rejection affirmed where using claimed elements in the manner suggested by the prior art necessarily resulted in claim-recited effect).

We acknowledge the disclosures in Yang, Sugano, Yamasaki, and Cook '072 (*see* FF 10-17). While it might be true that Sugano and Yamasaki disclose that CLA increases certain populations of immunoglobulins, Appellants do not point to any disclosure in either of these references, or Cook '072, specifically mentioning, much less disparaging, the treatment of rheumatoid arthritis with CLA.

We are therefore not persuaded that these references' disclosures are sufficient to refute the direct disclosures in both Cook and Horrobin of the desirability of treating rheumatoid arthritis with conjugated linoleic acid and/or its esters. To the contrary, Cook teaches the usefulness of CLA in treating rheumatoid arthritis despite explicitly acknowledging Yang's disclosure of the increase in proteinuria caused by CLA administration (FF 3).

We are therefore not persuaded that any of the Yang, Sugano, Yamasaki, or Cook '072 references, alone or in combination, would have dissuaded an ordinary artisan from treating rheumatoid arthritis with conjugated linoleic acid and/or its esters, as explicitly taught by Cook and Horrobin. We accordingly affirm the Examiner's rejection of claims 3 and 5 as being obvious over Cook and Horrobin.

Because they were not argued separately, claims 6-16 fall with claims 3 and 5. *See* 37 C.F.R. § 41.37(c)(1)(vii).

SUMMARY

We affirm the Examiner's rejection of the Examiner's rejection of claims 3 and 5-16 as being unpatentable under 35 U.S.C. § 103(a) over Cook and Horrobin.

TIME PERIOD

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED

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